A4

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,404	08/05/2002	Michaela Arndt	4121-135	1053

7590 03/13/2006

Steven J Hultquist
Intellectual Property Technology Law
PO Box 14329
Research Triangle Park, NC 27709

EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,404	ARNDT ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7-14,16-18,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 15, and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

2. Applicant's election with traverse of Group I, filed 01/13/2006, is acknowledged. The traversal is made on the following grounds: (1) the method of making and use of the antibody is not independent and distinct from the antibody of Group I; (2) searching the subject matter of antibody and method of making and using will not impose serious burden; (3) the prior art teachings of the Fv constructs do not disclose such construct are specific against tumor cells and inducing tumor cell lysis.

This is not found persuasive because inventions in Groups I-III have no special technical feature that defined in the contribution over the prior art teachings for the reasons of record set forth in the Office Action mailed 12/13/2005 which is hereby reiterated. Therefore, the inventions do not have a single general inventive concept and so lack unity of invention. Further, the search burden is not a consideration in applications entering the National Stage under 35 U.S.C. 371.

The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules for applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in MPEP Chapter 1800.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 1, 11-14 and 17 have been amended.
Claims 19-21 have been added.
Claims 1-21 are pending.

Claims 7-14, 16-18, 20 and 21 are withdrawn from further consideration by the Examiner under 37 C.F.R. 1.142(b) as being drawn to nonelected invention.

Claims 1-6, 15 and 19, read on an Fv antibody construct having binding site for CD16 and CD30, are currently under consideration.

3. Applicant's claim for domestic priority under 35 U.S.C. 371 is acknowledged. The priority application PCT/DE00/02589 upon which benefit is claimed appears to provide adequate support under 35 U.S.C. 112 for subject matter claimed in the instant application.

Applicant's provision of foreign priority documents GERMANY 19937264.0 is acknowledged.

However, English translations have not been provided. Therefore, it is not clear whether the foreign priority documents provide written description for the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. 112, first paragraph.

Therefore, the priority date of the instant claims is deemed to be the filing date of the priority application PCT/DE00/02589 (08/02/2000).

The specification on page 1, line 1 should include a specific reference to the priority application PCT/DE00/02589 for which benefit is sought and the status of the instant application is a 371.

4. Applicant's IDS, filed 06/07/2002, is acknowledged. References AC, AD, and AE have not been considered because English translations have not been provided.

5. The application is required to be reviewed and all spelling, TRADEMARK, and like error corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent application, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

6. Claims 2, 5, 15 and 19 are objected to because of the following informalities.

Claims 2 and 15 recite "NK cells". It is suggested that applicant amend the claims to recite the full name of the "NK cells".

Claim 19 recites "(a) a V_H domain of an antibody...". The specification as filed discloses only anti-CD16 antibody and anti-CD30 antibody. If applicant intends to include antibodies other than anti-CD16 antibody and anti-CD30 antibody, the claim may be subject to enablement and written description rejection under 35 U.S.C. 112, first paragraph.

Appropriate correction is required.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-6, 15 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-6, 15 and 19 are indefinite in the recitation of "CD16 receptor" and "CD30 surface protein" because it is not clear if the claims are drawn to CD16/CD30 themselves or other receptor/surface protein(s) for CD16/CD30.

Applicant is suggested to amend the claims to recite CD16/CD30 for clarity.

B) Claim 5 is indefinite in the recitation of "pKTD16-30" and "DEM 12960". However, the instant specification discloses on page 4 that the expression vector is "pKID16-30" with deposit "DSM 12960".

Applicant is invited to clarify the discrepancy between the claimed "pKTD16-30" and "DEM 12960" and the disclosure of "pKID16-30" and "DSM 12960" of the instant specification from a person in position to corroborate the fact that the claimed biological material is the same as disclosed in the specification as filed.

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the expression vector pKTD16-30 is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification.

Applicant is invited to clarify the discrepancy between the claimed "pKTD16-30" and "DEM 12960" and the disclosure of "pKID16-30" and "DSM 12960" of the instant specification from a person in position to corroborate the fact that the claimed biological material is the same as disclosed in the specification as filed.

While it is noted that applicant has indicated that the expression vector pKID16-30 was deposited with DSMZ under DSM 12960 (see page 4 of the specification as filed), the following requirements must still be met in order to fulfill the requirement of 37 CFR 1.801-1.809. (See MPEP 2402-2411).

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicant or someone associated with the patent owner who is in a position to make such assurances, or statement by an attorney of record over his or her signature, stating that the expression vector has been deposited under the Budapest Treaty and that the expression vector will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of the deposit, 5 years after the last request for a sample, or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806.

If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-6, 15 and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by Arndt et al. (Blood, 1999. 94; 8:2562-2568. Reference AI on IDS) (see entire document).

Arndt et al. teach that a bispecific diabody having binding sites for both CD16 and CD30 is able to specifically induce the lysis of a CD30 positive Hodgkin's lymphoma derived cell line by Natural Killer (NK) cells (see entire document, particularly Results on pages 2564-2565). Arndt et al. further teach that the bispecific diabody is a heterodimer of anti-CD16 and anti-CD30 fusion comprising the VH domain of one antibody connected by a short linker to the VL domain of another antibody (e.g. see page 2562 in particular). Furthermore, Arndt et al. teach that the Fv construct is expressed from expression plasmid pKID 16-30 (e.g. see left column on page 2563).

Therefore, the reference teachings anticipate the claimed invention.

13. Claims 1-5, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Hartmann et al. (Blood. 1997, 89;6:2042-2047) (see entire document).

Hartmann et al. teach an anti-CD16/CD30 bispecific antibody binds one arm to CD30, which is expressed on Hodgkin, and Reed-Sternberg cells and its second arm binds to CD16 on NK cells and is able to induce specific lysis of CD30 positive tumor cells (see entire document, particularly page 2042). Hartmann et al. further teach that the side effects such as HAMAs in the anti-CD16/CD30 bispecific antibody treatment can be resolved by using less immunogenic bispecific single chain antibody or diabodies (e.g. see page 2046 in particular).

Therefore, the reference teachings anticipate the claimed invention.

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-5, 15 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hartmann et al (Leukemia and Lymphoma. 1998, 31:385-392. Reference AG on IDS) in view of Holliger et al. (PNAS. 1993, 93:6444-6448).

Hartmann et al. teach that anti-CD16/CD30 bispecific antibody binds CD30 expressed on Hodgkin and Reed-Sternberg cells and CD16 on NK cells leading to specific tumor cell killing (see entire document, particularly pages 385-390).

Hartmann et al. does not teach an antiCD16/CD30 Fv construct with peptide linker.

However, methods of making Fv or diabodies that have the same antigen specificity but without Fc region were well know in the art at the time the invention was made. For example, Holliger et al. teach methods of making small bivalent and bispecific antibody fragments by linking the V_H and V_L of any two different antibodies A and B to form two different "cross-over" chains V_HA-V_LB and V_HB-V_LA via peptide linkers (see entire document, particularly page 6444).

Holliger et al. teach that antibody fragment are preferable to whole antibodies because the Fc region of antibodies can lead to illegitimate targeting to cells expressing Fc receptors (e.g. see left column on page 6444). Further diabodies are smaller in size than whole antibody and can facilitate penetration of tumors (e.g. see left column on page 6448).

It would have been obvious to the ordinary artisan at the time the invention was made to make bispecific anti-CD16/CD30 Fv construct. The ordinary artisan would have been motivated to produce the Fv construct in particular for treating human Hodgkin's lymphoma because it is well know in the art that Fv construct is beneficial over whole antibody in that it can avoid illegitimate targeting to cells expressing Fc receptors and can facilitate tumor penetration.

Giving the teachings of Hartmann et al. regarding the effect of bispecific antiCD16/CD30 antibody in treating Hodgkin's lymphoma, and the teachings of Holliger et al. providing methods of making diabodies without Fc region, the ordinary artisan at the time the invention was made would have had a reasonable expectation of producing antiCD16/CD30 Fv construct.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
February 23, 2006

PHILLIP GAMBEL, PH.D.
PRIMARY EXAMINER
TECH CENTER 1600
2/27/06